A Phase Ib Dose-Escalation Study of the HS990 Inhibitor SNX-5422 and Erlotinib in Patients with EGFR-Mutant Lung Cancer and Acquired Resistance to EGFR Tyrosine Kinase Inhibitors

Hana A. Yu,1 Martin Gutierrez,2 Gregory J. Rieley, Deena Graham, Natalie Busby, James M. Hinson, Jr,1 Everardus O. Orlemans1

1Memorial Sloan-Kettering Cancer Center, New York, NY; 2Hackensack University Medical Center, Hackensack, NJ; 3Unicorn Pharma Consulting, Brentwood, TN; 4Esanex, Inc, Indianapolis, IN

OBJECTIVES

Primary

- To determine the maximum tolerated dose (MTD) of SNX-5422 when given in combination with erlotinib in patients with EGFR-mutant NSCLC with acquired resistance to erlotinib.

Secondary

- To characterize the safety profile for the combination of SNX-5422 and erlotinib.
- To investigate the effects of SNX-5422 plus erlotinib on tumor response.

METHODS

Design

- Phase I, open label, 1:1 dose escalation study
- SNX-5422 dosing was started at 50 mg/m2 on week 1; escalation schedule of 75 mg/m2 and 100 mg/m2, respectively.
- Maximum tolerated dose (MTD) was defined as the highest dose level associated with no dose-limiting toxicity (DLT) observed in 5/10 patients.
- If MTD was not reached, dosing was escalated without a 100 mg/m2 gap.

Antitumor Activity

- Tumor response was assessed every 8 weeks using RECIST 1.1 criteria for solid tumors. Only patients with post-baseline tumor measurements were included in the calculation of best response.

Safety and Efficacy Analysis

- Adverse events, laboratory parameters, ECOG performance status, and antitumor activity were evaluated in all patients.

RESULTS

Antitumor Activity

- No objective responses were observed.
- Noteworthy stable disease was observed in 2 patients (14%) having stable disease for at least 9 months and are disease at the end of 4 months.
- Stable disease was observed as best response in 9 of 15 patients (60%), and 6 of 14 patients (43%) had stable disease at the end of 4 months.
- No disease progression was observed at the end of 4 months.

Safety and Efficacy Analysis

- Grade 3 or 4 treatment-emergent adverse events were observed in 6 (35%) of patients.
- Treatment-related adverse events were observed in all patients.

CONCLUSIONS

In patients with acquired resistance to erlotinib:

- The MTD of SNX-5422 was established at 50 mg/m2 in combination with erlotinib.
- SNX-5422 dosing is limited to 50 mg/m2 due to lack of dose–response relationship.

References